

**Department of Health and Human Services**

**OFFICE OF  
INSPECTOR GENERAL**

**Institutional Review Boards:**

**A Time for Reform**



**JUNE GIBBS BROWN  
Inspector General**

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# **EXECUTIVE SUMMARY**

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## **PURPOSE**

To summarize the challenges facing institutional review boards and to make recommendations for Federal oversight.

## **BACKGROUND**

### **Role of Institutional Review Boards**

Institutional review boards (IRBs) play vital roles in protecting human research subjects. They review initial research plans to make certain that the plans provide subjects with adequate opportunity to provide informed consent and do not expose subjects to unreasonable risks. They also conduct continuing review of approved research to ensure that human-subject protections remain in force. They carry out their initial and continuing review functions in accord with Federal regulations first established in the 1970s and applicable to all research funded by the U.S. Department of Health and Human Services or carried out on products regulated by the Food and Drug Administration.

### **This Summary Report**

This is a synthesis report. It draws on our broad inquiry of IRBs and on findings we presented in three parallel reports. Its overarching conclusion is that the long-established system for protecting human research subjects has vulnerabilities that threaten its effectiveness. In the report we highlight the major elements leading to this conclusion and offer recommendations for improvement. The recommendations are especially important in view of current Federal plans to increase significantly the numbers of human subjects participating in clinical trials, and proposals to give IRBs increased responsibility in the areas of genetics and confidentiality.

With this report, we offer a warning signal and a framework for a concerted response to it. We do not document, nor do we suggest that widespread harm is being done to human subjects. We recognize the strengths of the current system and seek to build on them to enhance human-subject protections.

### **Methodology**

Given our focus on the overall system of protections, we did not carry out audits of IRBs or investigations of particular cases. To help us understand the big picture, we conducted an extensive review of Federal records and pertinent literature; held interviews and group discussions with many Federal officials and with representatives of about 75 IRBs; visited IRBs at 6 academic health centers where extensive clinical research is taking place; attended IRB meetings; and accompanied FDA inspectors on IRB site visits.

## FINDINGS

### **The Effectiveness of IRBs Is in Jeopardy.**

**They Face Major Changes in the Research Environment.** The current framework of IRB practices was shaped in the 1970s in an environment where research typically was carried out by a single investigator working under government funding with a small cohort of human subjects in a university teaching hospital. In recent years, that environment has been changing dramatically as a result of the expansion of managed care, the increased commercialization of research, the proliferation of multi-site trials, new types of research, the increased number of research proposals, and the rise of patient consumerism. Each of these developments has presented major disruptions and challenges for IRBs. “Never before,” concluded one recent review, “has such a pressure-cooker atmosphere prevailed within the IRB system.”

**They Review Too Much, Too Quickly, with Too Little Expertise.** This is especially apparent in many of the larger institutions. Expanded workloads, resource constraints, and extensive Federal mandates contribute to a rushed atmosphere where sufficient deliberation often is not possible. At the same time, the IRBs frequently are hardpressed to gain access to the scientific expertise they need to reach informed judgments about the research taking place under their jurisdiction.

**They Conduct Minimal Continuing Review of Approved Research.** In the environment described above, continuing review often loses out. Even where there is the will, there often is not the time to go beyond the perfunctory obligations. A lack of feedback from other entities that oversee multi-site trials contributes to the problem. The result is that IRBs have all too little information about how the informed consent process really works and about how well the interests of subjects are being protected during the course of research.

**They Face Conflicts That Threaten Their Independence.** Clinical research provides revenue and prestige to the institutions to which many IRBs belong. The institutions expect IRBs to support these interests at the same time that they protect human subjects. The resulting tension can lessen the IRBs’ focus on their basic mission. The minimal “outside” representation that typically exists on IRBs deprives them of an important counterbalance to the institutional interests. For independent IRBs, the dependence on revenue from industry sponsors exerts similar possibilities for conflict.

**They Provide Little Training for Investigators and Board Members.** The IRB system depends heavily on research investigators’ commitment to uphold human-subject protections. But as that system now operates, it offers little educational outreach to investigators to help them become informed and sensitized about these protections. Similarly, it provides minimal orientation and continuing education for IRB members--a deficiency that is especially detrimental to nonscientific and noninstitutional members.

**Neither IRBs Nor HHS Devote Much Attention to Evaluating IRB Effectiveness.** IRBs rarely conduct inquiries to determine how well they are accomplishing their mission; their judgments of effectiveness rely mainly on the number of protection lapses or complaints that are brought to their attention. The HHS agencies conducting oversight seldom go any further. The Office for Protection from Research Risks, in the National Institutes of Health, focuses almost entirely on upfront assurances. The Food and Drug Administration relies on compliance-focused inspections.

## **RECOMMENDATIONS**

With the above findings, we do not claim that there are widespread abuses of human research subjects. The current system of protections is supported by many conscientious research investigators committed to protecting human subjects and by many dedicated IRB members and staff doing their best under trying circumstances. A reviewer of this system can not help but be impressed by the contributions of these individuals, and the important function that IRBs have fulfilled over the past quarter of a century.

But our findings present an important warning signal. The capacity of IRBs to accomplish all that is expected of them is strained. In the years ahead, this difficult situation could become even worse in view of Federal plans to increase significantly the numbers of subjects in clinical trials and various proposals to give IRBs added responsibility in the areas of genetics and confidentiality. It is time, we believe, for reform.

Our recommendations offer a framework for such a response. We direct them jointly to the two HHS agencies responsible for IRB oversight: the Office of Protection from Research Risks (OPRR), which is located within the National Institutes of Health (NIH), and the Food and Drug Administration (FDA). These agencies oversee IRBs with different jurisdictions and operational approaches. It is essential, therefore, for them to collaborate closely if HHS as a whole is to respond effectively to the serious concerns that emerge from our inquiry. Below we present our general recommendations for the two agencies. In the text, we offer more explicit elaborations directed, as appropriate, to the particular agencies.

### **Recast Federal IRB Requirements So That They Grant IRBs Greater Flexibility and Hold Them More Accountable for Results.**

- ▶ Eliminate or lessen some of the procedural requirements directed to IRBs.
- ▶ Require that IRBs undergo regular performance-focused evaluations.

### **Strengthen Continuing Protections for Human Subjects Participating in Research.**

- ▶ Require Data Safety Monitoring Boards for some multi-site trials.

- ▶ Provide IRBs with feedback on developments concerning multi-site trials.
- ▶ Routinely provide IRBs with feedback about FDA actions against investigators.
- ▶ Require sponsors and investigators to notify IRBs of prior reviews of research plans.
- ▶ Call for increased IRB awareness of on-site research practices.

**Enact Federal Requirements That Help Ensure That Investigators and IRB Members Are Adequately Educated About and Sensitized to Human-Subject Protections.**

- ▶ Require that research institutions have a program for educating its investigators on human-subject protections.
- ▶ Require that investigators provide a written attestation of their familiarity with and commitment to human-subject protections.
- ▶ Require that IRBs have an educational program for board members.

**Help Insulate IRBs from Conflicts That Can Compromise Their Mission in Protecting Human Subjects.**

- ▶ Require more representation on IRBs of nonscientific and noninstitutional members.
- ▶ Reinforce to IRB institutions the importance of IRBs having sufficient independence.
- ▶ Prohibit IRB equity owners from participating in the IRB review process.

**Recognize the Seriousness of the Workload Pressures That Many IRBs Face and Take Actions That Aim to Moderate Them.**

- ▶ Require that IRBs have access to adequate resources.

**Reengineer the Federal Oversight Process.**

- ▶ Revamp the NIH/OPRR assurance process.
- ▶ Revamp the FDA on-site inspection process.
- ▶ Require the registration of IRBs.

## COMMENTS ON THE DRAFT REPORTS

Within the Department of Health and Human Services (HHS), we received comments on our four draft reports from the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and jointly from the Assistant Secretary for Planning and Evaluation (ASPE) and the Assistant Secretary for Health (ASH). We also solicited and received comments from the following external organizations: the Applied Research Ethics National Association (ARENA), the American Association of Medical Colleges (AAMC), the Consortium of Independent Review Boards (CIRB), and Public Citizen's Health Research Group. We include the detailed text of their comments and our responses to them in appendix D. Below we summarize the major thrust of both their comments and our responses. We made a number of changes in the final reports. Most were technical in nature. Their comments sought to clarify certain findings and a few involved clarifications and elaborations concerning the recommendations.

### NIH, FDA, and ASPE/ASH Comments

The HHS parties viewed the reports as raising important issues and recommendations warranting widespread discussion. They suggested various ways this could be accomplished. The NIH expressed particular support for our recommendation calling for the assurance process to be revamped so that it rests essentially on an institutional attestation to conform to IRB requirements and thereby enables OPRR to focus more on performance assessment and education. The FDA expressed reservations about refocusing its compliance-oriented inspection process, which it regards as having "great value," to one that is more performance-oriented. The FDA also raised concerns about the resource implications of some of our recommendations.

*We will support efforts to engage broadly-based dialogue on our findings and recommendations. At the same time, we underscore the importance of practical near-term actions that can be taken to address the vulnerabilities we point out. We particularly urge that FDA and NIH incorporate into their oversight specific lines of inquiry to determine how well IRBs are actually protecting human subjects. This would call for examining such matters as how the processes of recruiting, selecting, and gaining informed consent from human subjects actually work. It would also call for addressing verification efforts to make sure that protocols are in fact submitted for review and that approved protocols do not stray off course. On the matter of resources, we agree that this is an important issue warranting serious attention in the research and policy communities, particularly in view of added responsibilities IRBs may well face in the years ahead.*

### External Organizations' Comments

While the external parties supported many of our findings and recommendations, they also raised some strong concerns. Basically, these involved differences of substance and objections to the use of certain terms and language. In regard to the former, Public

Citizen, in expressing considerable alarm over our findings, felt that we should have gone further with our investigations and recommendations. On the other hand, ARENA and AAMC had reservations about our call for performance-focused evaluations and for more outside representation on IRBs. They were also concerned that a more active IRB role in conducting continuing review could undermine the trust that has existed between IRBs and the research community. With respect to the language we used, ARENA, AAMC, and CIRB called for a more precise use of a number of terms. The ARENA indicated that our use of the term “IRB oversight” was particularly misleading. The ARENA and AAMC both indicated that some of our wording was unduly alarmist and more encompassing than our methodology warranted.

*To facilitate a serious examination of the matters of substance we raise, we changed some of the language we used in the draft reports. Most notably, instead of referring to “IRB oversight,” we focused on IRB responsibilities and authorities to conduct “continuing review,” as specified in Federal regulations. But, this and various other such textual modifications we made in no way lessen our assessment that the effectiveness of the IRB system is in jeopardy. Our wide ranging and in-depth inquiry offers us ample basis to sound that warning. With respect to concerns raised that focus more strictly on matters of substance, we must underscore that if IRBs are to meet the significant challenges they face in the years ahead, they must become more fully accountable to the public. Trust in the investigators performing research is vitally important, but in itself is insufficient. The IRBs and Federal oversight agencies must find more effective and open ways of verifying that the consumer protection mission of IRBs is in fact being accomplished. This is especially important as the research environment in which IRBs function becomes increasingly commercialized.*